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Original Research Paper

Fenugreek: A therapeutic complement for patients with borderline hyperlipidemia: A randomised, double-blind, placebo-controlled, clinical trial

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ABSTRACT

Objective: Fenugreek (*Trigonella foenum-graecum*) is a medicinal plant from Fabaceae family. This clinical study was designed to evaluate the effects of Fenugreek seeds supplementation on serum biochemical parameters of patients with borderline hyperlipidemia.
Materials and methods: A randomised, double-blind, placebo-controlled clinical trial was conducted on 56 patients with borderline hyperlipidemia that were divided in two groups: F group received 8 g Fenugreek seeds powder sachets and P group received placebo sachets daily for 8 weeks. After 2 months, triglycerides (TG), total cholesterol (TC), low-density lipoprotein (LDL), high-density lipoprotein (HDL), fasting blood glucose (FBG) and body mass index (BMI) were evaluated and compared with the baseline.
Results: After 2 months, TG, TC, LDL and FBG significantly decreased in F group in comparison with P group, but these changes were not significant in HDL and BMI.
Conclusion: Our findings showed that Fenugreek seeds supplementation, as a phenolic-rich herb can be effective in the reduction of some lipid profile in patients with borderline hyperlipidemia.

1. Introduction

Dyslipidemias, a kind of disorder of lipid metabolism, are common worldwide and are characterised by increased plasma levels of the various lipid and lipoprotein fractions including total cholesterol and low-density lipoprotein (LDL), very low-density lipoprotein (VLDL), triglycerides, chylomicrons and their effects on cardiovascular disorders [1].

Hypercholesterolemia and the level of LDL have an important role in development of cardiovascular disease (CVD) and the reduction thereof can assist in the management of cardiovascular disease. Despite the diverse lipid-lowering drugs such as statins (3-hydroxy-3-methylglutaryl coenzyme A reductase) for the control of hyperlipidemia, a significant number of patients do not reach their LDL target points and the side effects of these drugs have been reported in some studies [2–4]. To expedite the reduction of LDL cholesterol, higher doses of statins can be administered. However, even with high doses of statins, atherogenic dyslipidemia is not completely reversed. For this reason, other approaches to the treatment of combined hyperlipidemia may be considered [5]. On the other hand, in recent years, herbal medicines such as *Melissa officinalis*, *Silybum marianum*, *Anethum graveolens* and *Rhus coriaria* have been used for management of hyperlipidemia [6–8]. Nowadays, there is an increase in the interest in dietary bioactive compounds that protect humans against several diseases and/or reduce their intensity [9]. Fenugreek (*Trigonella foenum-graecum*) belongs to Fabaceae family. It is a highly antioxidant and phenolic-rich food that contains flavonoids, such as kaempferol 3-O-glycoside, apigenin-7-O-rutinoside, and naringenin. The effects of these phenolic compounds in hyperlipidemia have been demonstrated in the literature [10,11]. Therefore, studies aimed to find complementary and alternative way to treatment diseases with much more efficacy and less adverse effects for normalisation of lipid profile seems to be essential.

Abbreviations: BMI, body mass index; CVD, cardiovascular disease; FBS, fasting blood sugar; HDL, high density lipoprotein; LDL, low-density lipoprotein; TG, triglycerides; SCFAs, short-chain fatty acids; TCH, total cholesterol; VLDL, very low-density lipoprotein.

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2. Material and methods

2.1. Study design

A parallel, randomised, double-blind and placebo-controlled clinical trial was conducted, with the participation of 56 patients with hyperlipidemia (conducted in Besat Nahaja Hospital, Tehran, Iran between January and March 2014). This study was approved by Medical Ethics Commission in Qazvin University of Medical Sciences and registered in the Iranian Registry of Clinical Trials at (http://www.irct.ir) with the IRCT2013111815452N1 and reported as CONSORT criteria. This study was conducted in accordance with the Declaration of Helsinki.

2.2. Plant extraction and bioactive screening

For the Fenugreek powder extract, 100 g of Fenugreek sachets were weighed and water:methanol (30:70) was added. The solution was stirred at 100 rpm for 24 h at room temperature. Then, the extract was filtered by paper, transferred into a flask and dried using a rotating evaporator at 40 °C. Finally, extract was stored at 6 °C to prevent compound degradation until analysis. The Folin-Ciocalteu technique was used for total phenol content characterisation [12]. Therefore, 50 μL of extract was assayed with 250 μL of Folin reagent and 500 μL of Na_2CO_3 (20%, w/v). The mixture was diluted with double distilled water to obtain final volume of 5 mL. Finally, the extract was incubated for 1 h at 27 °C and was then measured at 765 nm by a spectrophotometer. Gallic acid, as a standard, was used for concentration calculating and the results were expressed as gallic acid equivalents per gram of extract.

2.3. GC-MS analysis of Fenugreek seeds

Analyses were carried out on a Hewlett-Packard 5890 Series II included gas chromatograph interfaced to a Hewlett Packard 5989B mass spectrometer. Separations were performed on Ultra 1 (49 m 0.20 mm I.D., 0.11 mm, Hewlett-Packard) and DB-Wax (60 m 0.25 mm I.D., 0.25 mm) capillary columns. Helium was used as a carrier gas (1.0 mL/min C.F.) and the oven temperature was programmed as 65°–230 °C with a heating rate of 2 °C/min. Injector and interface temperatures were 230 °C and 250 °C, respectively. EI mass spectra were recorded at 70 V ionisation voltages over the mass range 40–400. Samples (0.5 mL of oil solutions 1:10 in hexane) were injected by split injection (1:33).

2.4. Inclusion criteria

The inclusion criteria: greater than 18 years and less than 65 years old; an experiment with one of the following factors related to dyslipidemia: LDL >135 mg and <190 mg/dl; high density lipoprotein (HDL) <40 mg/dl; total cholesterol (TCH) >200 mg/dl; triglyceride (TG) >150 mg/dl.

2.5. Exclusion criteria

The exclusion criteria: having underlying diseases such as diabetes, ischaemic heart disease (IHD), hypertension, metabolic syndrome, peripheral vascular disease, history of coronary artery disease; patients who used anti-hyperlipidemic agents, steroids; cigarette; alcohol; the patients with LDL level ≥190 mg/dl that need to medical treatment (for healthy people or with one risk factor); patients who may undergo unpleasant complications during the study including headache, vertigo, nausea and Fenugreek intolerance.

2.6. Drug design

The 8 g of Fenugreek seeds sachets were provided from Dineh Pharmaceutical Company, Tehran, Iran and the sachets containing starch as placebo in the same shape, size and colour were prepared by a pharmacist and packed in the same style container with a code. All sachets obtained either 8 g with the powder of Fenugreek or 8 g starch. Moreover, all containers were labelled as A or B.

2.7. Randomisation

The randomisation allocation sequence was generated by a statistician with SAS 9.2 statistical software PROC PLAN. The statistician for the randomisation did not participate in the study. Because all participants received both interventions (F and P groups), limitation such as blocking were unnecessary. Subjects complying with selection criteria were assigned a randomisation number taken from a randomisation list following the chronological order by which they were included, after verifying compliance with inclusion and exclusion criteria. The randomisation list remained closed until the end of the experimental intervention and registering data had finished. Blinding was sustained using matching placebo sachets that did not differ from the F sachets with regard to appearance or any other physical characteristics. All sachets were presented in opaque pack plastic packaging, and were delivered face-to-face at the beginning of each intervention period by the physician. The kind of drugs or placebo was not recognisable for patient or administrative of this study. Compliance treatment monitoring was measured with a questionnaire filled in by patients at a clinical interview, and the sachets bag bottles were returned afterwards. Consumption of >85% was considered an acceptable level of adherence.

2.8. Interventions

All the 56 patients were divided into 2 groups randomly: Fenugreek group (F group) and placebo group (P group) through sortation cards, in randomised and blind fashion (Fig. 1). The F group obtained Fenugreek sachets (8 g of Fenugreek seed powder, Dineh Pharmaceutical Company, Tehran, Iran) and P group received placebo sachets (8 g starch powder) with the lunch meals for 8 weeks (the usage of drugs was explained for each patient individually). The patients followed up to control in terms of use sachets, response to the relevant questions, and prevention of sample loss and to receive sachets for the next month was done via monitoring the patients referring to Besat Nahaja Hospital. Likewise, the participants were advised to not change their usual diet, self-reliant changes of their drugs doses and physical activities during the intervention and use of other same products.

2.9. Measurements

Demographic data including age, BMI, gender, marital status, medical and drug history were evaluated and recorded through interview at the baseline and 8 weeks after the intervention with the patients. The patients' weight by a scale with 100 g error and with light clothing, height, in standing position without shoes by a height-measurer with 1 cm error were measured before and 8 weeks after study and calculated BMI with relevant formula. After 12–14 h of fasting, 10 mL sample of venous blood was taken from each patient by laboratory technician at baseline and end of the intervention. The centrifuge of samples was performed at the room temperature and at 3000 rpm for 10 min to separate serum. FBG was assessed using an enzymatic (glucose oxidise-peroxides) in vitro test. Serum total cholesterol, TG, LDL and HDL levels were measured by enzymatic colorimetric analysis. All of tests used

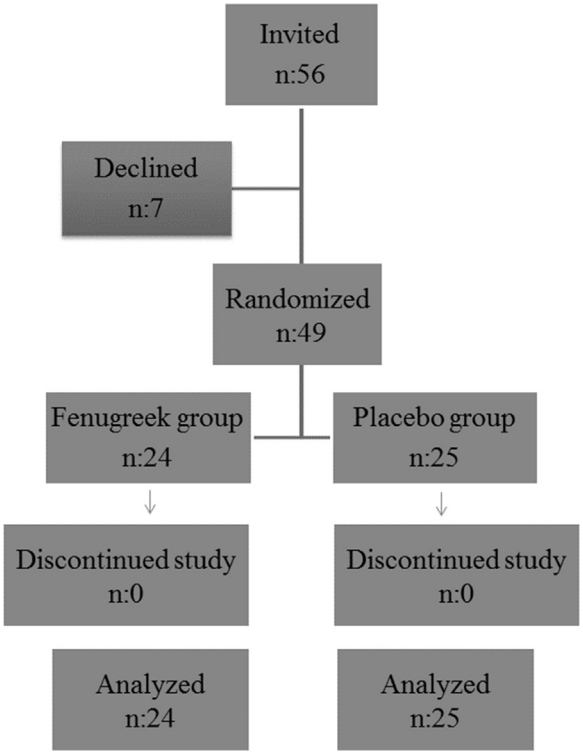

Fig. 1. Flow chart of the study participants.

Table 1
Chemical compounds detected in Fenugreek by GC/MS.

No.	Compounds	RI[a]	% %
1	Germacrene-D	1461	28.2
2	Bicyclogermacrene	1508	27.1
3	Viridiflorol	1563	5.9
4	β-caryophyllene	1409	5.6
5	Spathulenol	1561	4.1
6	Carvone	1260	2.5
7	Allo-aromadendrene	1459	2
8	Ledol	1611	1.9
9	Caryophyllene oxide	1561	1.4
10	α-cadinol	1672	1.4
11	δ-cadinene	1529	1.2
12	β-elemene	1403	1.1
13	β-bourbonene	1381	1
14	*n*-dodecane	1197	1
15	terpinene-4-ol	1204	0.9
16	valeranone	1692	0.8
17	α-pinene	933	0.7
18	Trans-β-ionone	1499	0.5
19	α-thujone	1110	0.4
20	α-terpineol	1189	0.4
21	Tau-muurolol	1644	0.3
22	Mintsulfide	1737	0.3
23	β-copaene	1420	0.3
24	α-copaene	1411	0.3
25	Bornylacetate	1309	0.3
26	Palustrol	1563	0.2
27	*n*-tetradecane	1431	0.2
28	Borneol	1161	0.2
29	Heptadecane	1692	0.1
30	Limonene	1067	0.1

[a] RI, retention Kovats indices.

standard enzymatic kits produced by the BIONIC Company, Tehran, Iran with Hitachi Auto analyzer device, Tokyo, Japan.

2.10. Sample size

To detect differences between the two interventions (F and P groups) of TC 20 mg/dl under $\alpha = 0.05$ bilateral significance level, power of study 85% and the sample size was 49 participants.

2.11. Statistical analysis

Statistical analysis was performed with SPSS version 21 (SPSS Inc., Chicago, IL, USA). For determining of quantitative data distribution, Kolmogorov–Smirnov test was used. The results of the quantitative data with normal distribution were reported as mean ± SD. Paired samples *t*-test was applied to identify the differences between the conditions before and after measurements and two independent samples *t*-test was used for the analysis of differences between the groups. *P*-values ≤0.05 were considered significant.

2.12. Results

After the GC-MS analysis of Fenugreek seeds essential oils, 30 chemical compounds were identified in this herb (Table 1). The most abundant constituents in this plant were germacrene-D, bicyclogermacrene, viridiflorol and β-caryophyllene with 28.2, 27.1, 5.9 and 5.6 percentages. The extract analysis in this herb indicated that the polyphenols includes most abundant constituents of this plant (112.7 mg gallic acid equivalents/g dry weight extracts). Among the study, 7 patients (out of 56) had left the study according to personal reasons. Finally, 49 participants completed this study that 24 patients in F group including: 11 females (45.8%) and 13 males (54.2%) and 25 patients in P group including: 12 females (48%) and 13 males (52%) accomplished this trial. The average ages in this study were 37.22 y ± 11.73 y and 38.07 y ± 11.79 y in F and P group, respectively. The baseline LDL, HDL, TCH, TG, FBS, BMI, LDL: HDL and TCH:HDL in two groups were assessed with no significant differences between the two groups ($P \geq 0.05$) (Table 2). Biochemical parameters of participants in F and P groups including FBS, LDL, HDL, TC, TG, LDL:HDL, TCH: HDL and BMI have been shown at the baseline and the end of study (Table 3). The results of this intervention showed a significant difference in TG and FBS ($P \leq 0.05$), LDL ($P \leq 0.01$) and TCH ($P \leq 0.001$) between two groups after the study, but there were no significant differences between two groups in HDL, TCH: HDL, LDL: HDL and BMI ($P \geq 0.05$). There were significantly reductions in TG, LDL, FBS and TC in F treated vs. placebo group after 8 weeks when compared

Table 2
Baseline characteristics of patients in Fenugreek and placebo groups.

Variables	F group Mean ± SD	P group Mean ± SD	*P*-value
Age (year)	37.22 ± 11.73	38.07 ± 11.79	0.79
TG mg/dl	209.75 ± 81.92	208.11 ± 103.46	0.95
TC mg/dl	208.33 ± 27.20	210.89 ± 53.11	0.76
LDL mg/dl	123.82 ± 33.46	135.89 ± 41.63	0.12
HDL mg/dl	41.19 ± 7.66	42.89 ± 10.13	0.84
FBS mg/dl	95.52 ± 5.91	96.33 ± 11.02	0.25
LDL/HDL	2.96 ± 0.78	2.16 ± 0.80	0.19
TCH/HDL	5.057 ± 0.16	3.87 ± 1.07	0.06
BMI kg/m2	27.42 ± 3.46	27.59 ± 2.28	0.81
Gender	*N* (%)	*N* (%)	
Female	11 (45.8)	12 (48)	0.68
Male	13 (54.2)	13 (52)	

Table 3
Comparison of variables before and after the intervention in Fenugreek and placebo groups.

Variables	F group Mean ± SD		*P*-value	P group Mean ± SD		*P*-value
	Before	After		Before	After	
TG	209.75 ± 81.92	202.2 ± 83.09	0.042*	208.11 ± 103.46	207.04 ± 38.16	0.062
TCH	208.33 ± 27.20	206.32 ± 19.12	0.003***	210.89 ± 53.11	211.32 ± 34	0.96
LDL	123.82 ± 33.46	129.74 ± 26.71	0.01**	135.89 ± 41.63	135.84 ± 25.67	0.16
HDL	41.19 ± 7.66	41.54 ± 7.86	0.65	42.89 ± 10.13	43.71 ± 9.54	0.46
FBS	95.52 ± 5.91	93.13 ± 2.3	0.04*	96.33 ± 11.02	95.85 ± 10.15	0.32
LDL/HDL	2.96 ± 0.78	2.97 ± 0.66	0.91	2.16 ± 0.80	2.24 ± 0.73	0.43
TCH/HDL	5.057 ± 0.16	5.04 ± 0.88	0.9	3.87 ± 1.07	3.74 ± 0.95	0.36
BMI	27.42 ± 3.46	27.28 ± 3.32	0.25	27.59 ± 2.28	27.43 ± 2.37	0.18

BMI, body mass index; FBS, fasting blood sugar; HDL, high-density lipoprotein; LDL, low-density lipoprotein; TCH, total cholesterol; TG, triglyceride.
* Significant in $P \leq 0.05$.
** Significant in $P \leq 0.01$.
*** Significant in $P \leq 0.001$.

with baseline. The reductions in F group were 7.55, 3.08, 2.39 and 2.01 mg/dl in TG, LDL, FBS and TC, respectively compared with baseline. However, such an effect was not observed in the P group. Although the reductions in HDL, TCH: HDL, LDL: HDL and BMI was not significant ($P \geq 0.05$).

3. Discussion

In many hyperlipidemic patients, maintaining lipid profiles in an optimal range is difficult and prescribing several drugs from different pharmacological classes of anti-hyperlipidemic agents with high dosage is frequently needed. Increasing the number and dosage of drugs enhances the possibility of developing medical side effects but reduces patient's compliance. On the other hand, discontinuation of treatment is not far-fetched [13]. At the present time, introduction of some adjunctive therapies, such as herbal therapies seems sensible.

Fenugreek seeds are polyphenol-rich foods that other studies suggest, in concert with our results that may improve lipid profile and reduce risk factors possibly due the high values of polyphenol in this herb. 4-Hydroxyisoleucine, as one of the Fenugreek chemical compounds, can play an important role in TG reduction that has been shown in previous studies [14,15]. Other phenolic compounds like apigenin, caffeic acid, gallic acid, luteolin and naringenin have been reported from this plant in previous studies [16,17]. The essential oil analysis showed that the most abundant essential oil is germacrene-D (28.2%) and the effects of this natural sesquiterpene on hyperlipidemia have been reported in many studies [8]. On the other hand, the antihyperlipidemic effects of bicyclogermacrene as a potent natural product in hyperlipidemia control in *Casearia sylvestris* were shown [18]. As a result, the effects of fermentation products of Fenugreek fibre such as short chain fatty acids (SCFAs) (acetate, propionate, and butyrate) could also be considered in the amelioration of diabetic and hyperlipidemic status. Fenugreek, like another herb that is phenolic-rich herb could improve hyperlipidemia and the cardiovascular system. Apigenin, luteolin and gallic acid from Sumac, Artichoke and Hibiscus and their improvement effects in hyperlipidemia have been reported in many studies [9,19,20]. The chemical compounds reported from Fenugreek too [21]. As the results showed, after 8 weeks of Fenugreek in 8 g sachets, TG, TC, LDL and FBG significantly reduced. However, we did not identify any significant difference in BMI, HDL, LDL/HDL and TC/HDL before and after the intervention in F group. The reduction between before and after the intervention in TG in F group was 7.55 mg/dl, while this reduction in P group was 1.07 mg/dl. In TC factor the reduction between before and after the intervention in F group was 2.01 mg/dl, while in P group 0.43 mg/dl was increased. The reductions between before and after the intervention in LDL and FBS in F group were 3.08 and 2.39 mg/dl, respectively, and the reductions in P group were 0.05 and 0.48 mg/dl respectively. The significant differences between the reductions in F and P group are completely clear. However, the differences between two groups before and after the study in HDL, LDL/HDL, TC/HDL and BMI were not significant. Indeed, beneficial antioxidant effects of this herb could modulate the lipid profiles [22].

4. Conclusion

This clinical study showed that consumption of 8 g Fenugreek seed powder per day in patients with borderline lipid profiles for two months could improve serum TG, TC, LDL and FBG levels. Without causing any considerable side effect, Fenugreek seeds were shown to be an effective therapeutic adjuvant in hyperlipidemia. Furthermore, the effects of Fenugreek could be attributed to phenolic compounds as the dominant constituents in this herb. However, further research is required to clarify the mechanisms behind these observations.

Conflict of interests

All authors approved the final version of the manuscript, and none of the authors declared a conflict of interest.

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References

[1] D.E. Casey, Dyslipidemia and atypical antipsychotic drugs, J. Clin. Psychiatry 65 (Suppl. 18) (2004) 27–35.
[2] D. Kiortsis, P. Giral, E. Bruckert, G. Turpin, Factors associated with low compliance with lipid-lowering drugs in hyperlipidemic patients, J. Clin. Pharm. Ther. 25 (6) (2000) 445–451.
[3] V.G. Athyros, A.A. Papageorgiou, V.V. Athyrou, D.S. Demitriadis, A.G. Kontopoulos, Atorvastatin and micronized fenofibrate alone and in combination in type 2 diabetes with combined hyperlipidemia, Diabetes Care 25 (7) (2002) 1198–1202.
[4] C.V. Rizos, F. Barkas, M.S. Elisaf, Reaching low density lipoprotein cholesterol targets, Curr. Med. Res. Opin. 30 (10) (2014) 1967–1969.
[5] S. Kianbakht, B. Abasi, M. Perham, F. Hashem Dabaghian, Antihyperlipidemic effects of *Salvia officinalis* L. leaf extract in patients with hyperlipidemia: a

randomized double-blind placebo-controlled clinical trial, Phytother. Res. 25 (12) (2011) 1849–1853.
[6] V. Hajhashemi, N. Abbasi, Hypolipidemic activity of *Anethum graveolens* in rats, Phytother. Res. 22 (3) (2008) 372–375.
[7] K. Abascal, E. Yarnell, The many faces of *Silybum marianum* (Milk Thistle): part 2 – clinical uses, safety, and types of preparations, Altern. Complement. Ther. 9 (5) (2003) 251–256.
[8] P. Jandaghi, M. Noroozi, H. Ardalani, M. Alipour, Lemon balm: a promising herbal therapy for patients with borderline hyperlipidemia—a randomized double-blind placebo-controlled clinical trial, Complement. Ther. Med. 26 (2016) 136–140.
[9] H. Ardalani, M.H. Moghadam, R. Rahimi, J. Soltani, A. Mozayanimonfared, M. Moradi, A. Azizi, Sumac as a novel adjunctive treatment in hypertension: a randomized, double-blind, placebo-controlled clinical trial, RSC Adv. (2016).
[10] O. Belguith-Hadriche, M. Bouaziz, K. Jamoussi, A. El Feki, S. Sayadi, F. Makni-Ayedi, Lipid-lowering and antioxidant effects of an ethyl acetate extract of fenugreek seeds in high-cholesterol-fed rats, J. Agric. Food Chem. 58 (4) (2010) 2116–2122.
[11] M. Sajty, L. Jackova, L. Merkovska, L. Jedlickova, J. Fedacko, M. Janicko, M. Vachalcova, R. Singh, Fenugreek seeds decrease oxidative stress and blood lipids and increase nitric oxide in patients with hyperlipidemia, Atherosclerosis 235 (2) (2014) e113.
[12] V. Singleton, J.A. Rossi, Colorimetry of total phenolics with phosphomolybdic-phosphotungstic acid reagents, Am. J. Enol. Vitic. 16 (3) (1965) 144–158.
[13] A.J. Wood, W.E. Evans, H.L. McLeod, Pharmacogenomics—drug disposition, drug targets, and side effects, New Engl. J. Med. 348 (6) (2003) 538–549.
[14] L. Jetté, L. Harvey, K. Eugeni, N. Levens, 4-Hydroxyisoleucine: a plant-derived treatment for metabolic syndrome, Curr. Opin. Investig. Drugs (London, England: 2000) 10 (4) (2009) 353–358.
[15] S. Fuller, J.M. Stephens, Diosgenin, 4-hydroxyisoleucine, and fiber from fenugreek: mechanisms of actions and potential effects on metabolic syndrome, Adv. Nutr.: Int. Rev. J. 6 (2) (2015) 189–197.
[16] S. Kaviarasan, K. Vijayalakshmi, C. Anuradha, Polyphenol-rich extract of fenugreek seeds protect erythrocytes from oxidative damage, Plant Foods Hum. Nutr. 59 (4) (2004) 143–147.
[17] O. Belguith-Hadriche, M. Bouaziz, K. Jamoussi, M.S. Simmonds, A. El Feki, F. Makni-Ayedi, Comparative study on hypocholesterolemic and antioxidant activities of various extracts of fenugreek seeds, Food Chem. 138 (2) (2013) 1448–1453.
[18] T. Schoenfelder, C.T. Pich, R. Geremias, S. Ávila, E.N. Daminelli, R.C. Pedrosa, J. Bettiol, Antihyperlipidemic effect of *Casearia sylvestris* methanolic extract, Fitoterapia 79 (6) (2008) 465–467.
[19] C.C. Chen, F.P. Chou, Y.C. Ho, W.L. Lin, C.P. Wang, E.S. Kao, A.C. Huang, C.J. Wang, Inhibitory effects of *Hibiscus sabdariffa* L extract on low-density lipoprotein oxidation and anti-hyperlipidemia in fructose-fed and cholesterol-fed rats, J. Sci. Food Agric. 84 (15) (2004) 1989–1996.
[20] R. Bundy, A.F. Walker, R.W. Middleton, C. Wallis, H.C. Simpson, Artichoke leaf extract (*Cynara scolymus*) reduces plasma cholesterol in otherwise healthy hypercholesterolemic adults: a randomized, double blind placebo controlled trial, Phytomedicine 15 (9) (2008) 668–675.
[21] S. Khole, S. Chatterjee, P. Variyar, A. Sharma, T. Devasagayam, S. Ghaskadbi, Bioactive constituents of germinated fenugreek seeds with strong antioxidant potential, J. Funct. Foods 6 (2014) 270–279.
[22] B. Annida, P. Stanely Mainzen Prince, Supplementation of fenugreek leaves lower lipid profile in streptozotocin-induced diabetic rats, J. Med. Food 7 (2) (2004) 153–156300.